Coexisting renal artery stenosis and membranous glomerulonephritis. Is there a link?

Sir,
The association of renal artery stenosis (RAS) and nephrotic-range proteinuria is uncommon, being related to focal segmental glomerulosclerosis in contralateral kidney, hyper-reninemic state and malignant hypertension [1,2]. Its association with other glomerular nephropathies is anecdotal. We report a patient with renovascular hypertension (RVHT) and nephrotic-range proteinuria, in whom a membranous glomerulonephritis was diagnosed.

Case. A 43-year-old female was admitted because of malignant hypertension. She had a history of hypertension which had been diagnosed 8 years before and was treated with verapamil 240 mg/day and lisinopril 20 mg/day. On admission blood pressure was 230/135 mmHg without differences between her limbs. Physical examination showed fine cracklings on lung bases, absence of heart murmur or abdominal bruits and no peripheral oedema was detected. Laboratory tests revealed serum creatinine 88.4 μmol/l, potassium 3.7 mEq/l, total protein 45 g/l, albumin 22 g/l, blood haemoglobin 12.1 g/dl, and white blood cell count 6700 μl. Proteinuria was 12 g/day and urine sediment contained 25–50 red cells per high-power field with characteristics of glomerular haematuria. Serological evaluation for immunoglobulins, complement, ANA, ANCA, antiphospholipid antibodies, syphilis, cryoglobulins, hepatitis B and C virus and HIV antibodies were negative. EKG showed left ventricular hypertrophy and a chest X-ray showed bilateral interstitial oedema. Renal scintigraphy study showed a decreased right kidney perfusion. Baseline plasma renin activity was 0.2 ng/ml/h (reference value 0.3–2.8) and baseline aldosterone 249 pg/ml (reference value <150) but the captopril test was positive [7], showing plasma renin activity after captopril of 3.2 ng/ml/h and aldosterone 83 pg/ml. In order to rule out the presence of renovascular stenosis an arteriography was performed showing a typical beaded appearance of the right renal artery (Figure 1, top). Right kidney biopsy was done to find out the cause of
The association between the presence of RVHT and the nephrotic syndrome has been known for many years, although glomerular lesions have been poorly described [2,3]. A significant decrease of proteinuria has been reported following the correction of the renal artery stenosis by different methods and more recently percutaneous angioplasty of the renal artery [4,5].

The appearance of moderate to severe proteinuria in RVHT cases has been related to the presence of mesangial hyperplasia [6], as well as secondary focal segmental glomerulosclerosis in the contralateral kidney [2,3,7]. The pathogenic mechanism which favours the development of this glomerulopathy has been related to glomerular hyperfiltration in the non-stenotic kidney due to the increased generation of angiotensin II. More recently, increased levels of TGF-β due to the angiotensin II production have been found to be associated with the development of focal and segmental glomerulosclerosis, in addition to fibrointimal vascular proliferation and interstitial fibrosis [3]. The association of RVHT with other glomerulopathies is anecdotal. Leslie et al. reported a case of fibromuscular dysplasia and membrano-proliferative glomerulonephritis [8]. These authors considered that some cases of fibromuscular dysplasia might represent a response to local inflammation induced by the deposition of circulating immune complexes in glomeruli, vasa vasorum or intima of medium-sized arteries.

In our case, the severity of proteinuria led us to perform a renal biopsy which confirmed the presence of membranous glomerulonephritis. Other authors reported the association of membranous glomerulonephritis with renal artery thrombosis related to nephrotic syndrome with marked hypoalbuminaemia [9], but none was reported in the literature reviewed (MEDLINE: 1975–October 2000) in whom membranous glomerulonephritis was associated with RAS secondary to fibromuscular dysplasia. Although proteinuria partially improved after the administration of angiotensin-converting enzyme (ACE) inhibitors, it persisted at the nephrotic level and only abated after renal artery angioplasty, together with an intensified treatment with ACE-inhibitors and angiotensin II receptor antagonists.

Normal baseline plasma renin activity in presence of renovascular stenosis may be explained by the study of Muller et al. [10]. These authors found that baseline plasma renin activity did not discriminate between renovascular and essential hypertension. However, as we have seen in our patient, plasma renin values after captopril and its increase from baseline values were predictive.

Our case confirms that severe hypertension worsens proteinuria in proteinuria glomerular diseases. This experience suggests to us the potential implication of haemodynamic and, probably also non-haemodynamic mechanisms of proteinuria in the presence of renal artery stenosis and the beneficial effect of angioplasty and ACE inhibitor treatment. Moreover, in some cases a kidney biopsy could be indicated to rule out other immunological lesions, including membranous nephropathy as found in our patient.

Comment. RVHT affects approximately 40% of patients with hypertension of difficult management. In these cases, hypertension seems to be a consequence of the activation of the renin-angiotensin system caused by the stenotic kidney [1].

nephrotic proteinuria. It revealed membranous glomerulonephritis stage II.

Blood hypertension therapy was begun with fosinopril 20 mg/day, doxazosin 2 mg/day, clortalidone 25 mg/day and atenolol 50 mg/day, consequently blood pressure decreased to 140/80 and proteinuria to 5.6–3.1 g/24 h. Because of the persistence of proteinuria in nephrotic range, an angioplasty of the right renal artery was performed, leading to a good morphological outcome (Figure 1, bottom). Five months after the angioplasty, blood pressure remained at about 140/80 mmHg and proteinuria progressively diminished up to 1.2–1.5 g/24 h. During the following 24 months, mean blood pressure was 130/70 mmHg and proteinuria remained at the same level after treatment with irbesartan 300 mg/day, clortalidone 12.5 mg/day, enalapril 10 mg/day and doxazosin 4 mg/day.

![Fig. 1. Arteriography showing a typical beaded appearance with stenosis and poststenotic dilatations from its origin up to 4 cm long, ending in an aneurysm of 8–9 mm in diameter at the level of the bifurcation area of the right renal artery (top). Result after angioplasty (bottom).](image)

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